

# Pain extent is associated with pain intensity but not with widespread pressure or thermal pain sensitivity in women with fibromyalgia syndrome

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**Title Page**

**Pain Extent is Associated With Pain intensity but not With  
Widespread Pressure or Thermal Pain Sensitivity in Women With  
Fibromyalgia Syndrome**

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**Category article:** Brief Report

**Short title:** Pain extent areas in fibromyalgia syndrome

**Key words:** fibromyalgia, pain extent, pressure pain, sensitization

## 33 Abstract

34

35 **Introduction/Objective:** Widespread pain is considered a sign of central sensitization in people  
36 with chronic pain. Our aim was to examine whether pain extent, assessed from the pain drawing,  
37 relates to measures from quantitative sensory testing in fibromyalgia syndrome (FMS). **Methods:**  
38 Thirty women with FMS and no other co-morbid conditions completed pain drawings (dorsal and  
39 ventral view) and clinical and related-disability questionnaires. Pain extent and pain frequency  
40 maps were obtained from the pain drawings using a novel customized software. Pressure pain  
41 thresholds were assessed over the 18 tender points considered by the 1990 American College of  
42 Rheumatology criteria for FMS diagnosis and over two additional standardized points. Heat and  
43 cold pain thresholds were also assessed on the dorsal aspect of the neck, the dorsal aspect of the  
44 wrist, and the tibialis anterior. Spearman's correlation coefficients were used to assess the  
45 relationship between pain extent and quantitative sensory testing outcomes as well as clinical  
46 symptoms. **Results:** Larger extent of pain was associated with a higher pain intensity (dorsal area:  
47  $r_s=0.461$ ,  $P=0.010$ ; total area:  $r_s=0.593$ ,  $P=0.001$ ), younger age (ventral area:  $r_s=-0.544$ ,  $P=0.002$ ;  
48 total area:  $r_s=-0.409$ ,  $P=0.025$ ), shorter history of pain (ventral area:  $r_s=-0.367$ ,  $P=0.046$ ), and higher  
49 cold pain thresholds over the tibialis anterior muscle ( $r_s=-0.406$ ,  $P=0.001$ ). No significant  
50 association was observed between pain extent and the remaining outcomes. **Conclusions:** Pain  
51 drawings constitute an easy and accurate approach to quantify widespread pain. Larger pain extent  
52 is associated with pain intensity but not with signs of central sensitization in women with FMS.

53

54 **Key words:** fibromyalgia, pain extent, pressure pain, sensitization

55

# **Pain Extent is Associated With Pain intensity but not With Widespread Pressure or Thermal Pain Sensitivity in Women With Fibromyalgia Syndrome**

## **Introduction**

Fibromyalgia syndrome (FMS) is a disabling condition including widespread pain and fatigue, in addition to cognitive, physical and sleep disturbances. The mean worldwide prevalence of FMS is estimated at ~2.7% although it varies depending on the diagnostic criteria applied [1]. Although the etiology of FMS is debated, it is accepted that people with this condition exhibit hyper-excitability of the central nervous system [2].

Pain drawings are used to obtain an illustration of pain location and distribution in people with pain [3]. Several instruments are used to record the pain location and the most common method involves asking the patients to draw where they feel pain on a paper body chart [3,4]. The location of symptoms is heterogeneous in FMS since most patients report that localized pain was present before widespread pain. Some studies have shown through pain drawings that the widespread pain in FMS is formed by multiple regional painful areas and that the intensity of pain is associated with the number of painful body areas [5] and ratings of local pain [6]. Larger pain areas are thought to represent a clinical sign of central sensitization [7]. There is some evidence showing that enlarged pain areas are associated with more persistent and severe pain [8] and higher pressure sensitivity [9] in knee osteoarthritis suggesting that quantification of pain extent can assist clinicians to identify subjects with sensitization. Further, widespread pain was associated with self-perceived disability, depression and self-efficacy in chronic whiplash [10].

No previous study has investigated if larger pain extent is associated with central sensitization in FMS. Therefore, our aim was to examine whether pain extent relates to clinical variables, health status and quantitative sensory test measures in women with FMS.

81 **Methods**

82 **Participants**

83 Women diagnosed with FMS following the American College of Rheumatology (1990/2010)  
84 criteria participated. Since a combination of both ACR 1990 and 2010 criteria is recommended  
85 [11], patients were required to fulfill the 2010 ACR Criteria and also needed to present with 11/18  
86 tender points according to the 1990 ACR Criteria [11]. They were excluded if they presented with:  
87 1, co-morbid medical conditions; 2, endocrine disorders; 3, malignancy; 4, psychiatric illnesses; 5,  
88 medication drug usage other than analgesics or antidepressants; 6, previous history of surgery or  
89 whiplash injury. They were asked to avoid any analgesic or muscle relaxant 24 hours prior to the  
90 examination. No change was made to their prophylactic drug treatment. The study was approved by  
91 local Ethics Committee of Universidad Rey Juan Carlos (URJC 08-30-2014). All patients provided  
92 informed written consent prior to their inclusion.

93 **Self-reported data**

94 An 11-point numerical point rating scale (NPRS; 0: no pain; 10: maximum pain) was used  
95 to determine the current, the worst, and the lowest level of pain experienced the preceding week  
96 [12]. The Spanish version of the Fibromyalgia Impact Questionnaire (FIQ) was used to determine  
97 related-disability [13]. Higher scores of the questionnaire indicate more negative impact.

98 **Pain drawing**

99 Participants were instructed to complete a pain drawing by shading, with a pencil, the  
100 perceived extent and location of their symptoms on two paper body charts (ventral and dorsal body  
101 views). All paper pain drawings were scanned to digital format. The scanned images were manually  
102 aligned to a standardized digital body chart and the pain drawings were copied manually by two  
103 trained operators using an image analysis software (Inkscape V.0.48.5) [14]. Pain extent, reported  
104 as the total number of pixels within the digital encircled pain drawings and inside the body chart,  
105 was computed for each digitalized chart [15,16]. Pain extent was expressed as percentage of the

total body chart area (ventral: 21577 pixels, dorsal: 145675 pixels, total: 291978 pixels). Pain frequency maps were obtained by superimposing the pain drawings from all participants to illustrate the most frequently reported location of pain across the sample. A color grid was used to indicate the percentage of people that reported pain in a specific area.

#### **Quantitative Sensory Testing (QST)**

Pressure pain thresholds (PPT) were assessed with an electronic algometer (Somedic AB©, Farsta, Sweden). Patients were instructed to press the “stop-button” as soon as the pressure turned to pain. The mean of three trials on each point was used in the analysis. A 30sec resting period was allowed between trials. The reliability of algometry is high in patients with muscle pain [17]. PPT was measured bilaterally over the 18 tender point areas considered for FMS diagnosis and over the second metacarpal and tibialis anterior muscle in a random order.

Thermal pain thresholds over the dorsal aspect of the neck, the dorsal aspect of the wrist and the tibialis anterior muscle were tested with a Thermotest System (Somedic AB©, Farsta, Sweden). Patients were instructed to press a hand-controlled switch when the sensation change from heat/cold to heat pain/cold pain (heat or cold pain thresholds, HPT/CPT). The mean of 3 trials for each region was used for the analysis. A rest of 5 s was provided between trials.

#### **Sample size calculation**

Sample size calculation was based on detecting significant moderate correlations ( $r=0.6$ ) between the variables with an alpha level ( $\alpha$ ) of 0.05 and a desired power ( $\beta$ ) of 95%. This generated a sample size of at least 25 subjects.

#### **Statistical analysis**

Distribution of the data was tested with the Shapiro-Wilk test and non-normally distributed data were observed. Since no side-to-side differences in PPTs, HPTs or CPTs were found, the mean of both sides was used in the analysis. Spearman’s correlation coefficients were computed to reveal associations between pain extent with tender point count, pain intensities, related-disability, PPTs, HPTs and CPTs. Correlations were considered weak when  $r<0.3$ ; moderate when  $0.3<r<0.7$ , and

133 strong when  $r > 0.7$ . Statistical analyses were performed using SPSS 22 (SPSS Inc, Chicago, IL,  
134 USA). The significance level was set at  $P < 0.05$ .

135

## 136 **Results**

### 137 **Demographic and clinical data of the patients**

138 Thirty women with FMS (age:  $49.5 \pm 8.1$  years) were included. **Table 1** summarizes all data of the  
139 sample. The pain extent was  $16.2\% \pm 3.4\%$ ,  $13.3\% \pm 4.6\%$  in the ventral and  $19.3\% \pm 6.5\%$  in the  
140 dorsal body areas. Pain frequency maps are illustrated in **Figure 1**, whereas correlations between  
141 pain extent, clinical symptoms and measures of central sensitization are reported in **Table 1**.

### 142 **Pain extent and clinical symptoms**

143 Significant negative correlations were observed between pain extent and age (ventral area:  $r_s = -$   
144  $.0544$ ,  $P = 0.002$ ; total area:  $r_s = -0.409$ ,  $P = 0.025$ ) and pain duration (ventral area:  $r_s = -0.367$ ,  $P = 0.046$ ):  
145 larger pain extent was associated with younger age and shorter history of symptoms. Pain extent  
146 was positively correlated with the worst level of pain (dorsal area:  $r_s = 0.461$ ,  $P = 0.010$ ; total area:  
147  $r_s = 0.593$ ,  $P = 0.001$ ): the larger pain extent, the higher pain intensity. **Figure 2** illustrates the scatter  
148 plots showing the association between pain extent and the worst level of pain. No other association  
149 was found between pain extent and clinical features, including tender point count or disability.

### 150 **Pain extent and measures of central sensitization**

151 No significant associations were observed between pain extent and widespread PPT or HPT.  
152 Pain extent measured from the ventral body chart showed a significant negative correlation with  
153 CPT over the tibialis anterior muscle ( $r_s = -0.406$ ,  $P = 0.001$ ): the larger the pain extent, the lower the  
154 CPT.

155

## 156 **Discussion**

157       Pain extent was positively associated with the worst level of pain and negatively associated  
158 with age and years with pain in women with FMS: a larger distribution of pain correlated with  
159 higher intensity of their worst pain, younger age, or shorter history of pain. Pain extent was not  
160 associated with tender point count, pressure and thermal pain sensitivity (except CPT over the  
161 tibialis anterior) in this sample of women with FMS.

162       Although it is accepted that individuals with FMS exhibit widespread pain, the evaluation  
163 and the quantification of pain drawings in FMS is scarce. Pain frequency maps reported in our study  
164 indicate a widespread pain pattern in our sample of women with FMS. In fact, the pain extent  
165 values observed in our sample of FMS women were higher than those areas reported in woman with  
166 whiplash associated disorders [10]. Further, the pain frequency maps also showed that FMS patients  
167 reported pain in neck, shoulder, low back, elbow, or knee areas supporting previous assumptions  
168 that the overall widespread pattern suffered by people with FMS is the sum of multiple regional  
169 pain areas [5,6]. This hypothesis is supported by current ACR2010 preliminary diagnostic criteria  
170 where patients are required to report painful regions rather than widespread pain [18]. Nevertheless,  
171 although widespread pain is no longer required for FMS diagnosis according to the ACR2010  
172 diagnostic criteria, most patients (94%) suffered from widespread pain [18]. Therefore, it seems that  
173 the symptoms experienced by women with FMS are widespread, but localized in particular areas.  
174 Our study is the first to reveal that pain frequency maps show an overlap between the locations of  
175 the most frequent pain areas and tender point locations originally proposed and included in 1990  
176 classification criteria for FMS.

177       Pain extent was associated with younger age and shorter history of pain symptoms. Patient-  
178 reported improvements have been also previously correlated with younger age and shorter duration  
179 of FMS symptoms at diagnosis [19]. The reduction of pain extent could reflect a natural evolution  
180 of FMS where the pain is perceived more widespread during the first years and with time pain tends



181 to become more localized. This hypothesis agrees with long-term studies suggesting that a portion  
182 of patients with FMS usually experience improvement in symptoms with time [20,21].

183 In our study, pain extent was positively associated with the worst pain intensity experienced  
184 suggesting that clinical pain is associated with more widespread pain. These results agree with those  
185 previously observed in people with knee osteoarthritis where larger pain areas were associated with  
186 greater severity of pain [8,9]. The association between pain intensity and pain extent would provide  
187 indirect evidence for the role of peripheral input in FMS as previously suggested [5]. Persistent and  
188 long-lasting activity from peripheral nociceptive afferents can result in central sensitization that can  
189 exacerbate the magnitude of the overall widespread pain [5].

190 Pain extent was not associated with pressure or thermal pain sensitivity in our sample of  
191 women with FMS. We only found that more widespread pain was associated with cold hyperalgesia  
192 over the tibialis anterior muscle. Cold pain sensitivity has been previously reported in FMS [22].  
193 Cold hyperalgesia is considered a feature of neuropathic pain as result of peripheral nerve injury  
194 and there is evidence suggesting the concept of impaired small fibre function pointing towards a  
195 neuropathic nature of the pain in FMS [23]. One possible explanation for our findings may link  
196 widespread pain, younger age and shorter history of pain combined with a lower neuropathic  
197 involvement.

198 We explored, for the first time, the utility of the pain drawing to extract pain extent scores  
199 in FMS. The software used to compute pain extent eliminates estimation errors; nevertheless, there  
200 are some methodological issues that should be considered. First, we collected data from a sample of  
201 30 women, which may be considered a small sample. Second, although the assessment method has  
202 shown high reliability [15,16], information on the reliability of pain drawings specifically in FMS  
203 are not available. Third, we collected static outcomes of sensitization. We do not know if pain  
204 extent would be associated with dynamic outcomes such as wind-up, spatial/temporal summation,  
205 or conditioned pain modulation. Finally, we did not investigate the presence of psychological  
206 features that can be associated with higher pain extent [10] or abnormal pain drawings in

207 individuals with chronic pain [24]. Nevertheless, a recent review did not support the assumption  
208 that unusual pain drawings predict the presence of a disturbed psychological state [25].

209

## 210 **Conclusions**

211 This study showed that an expanded distribution of pain area was correlated with greater  
212 pain intensity, younger age, shorter history of symptoms and cold hyperalgesia detected over the  
213 tibialis anterior muscle in women with FMS. Pain extent was not associated with tender point count,  
214 pressure or heat hypersensitivity. Pain drawings may constitute an easy and accurate approach for  
215 quantification of widespread pain although their ability to identify central sensitization in FMS is  
216 questionable.

217

## 218 **Disclosures**

219 M Barbero, C Fernández-de-las-Peñas, M Palacios-Ceña, C Cescon and D Falla, authors of  
220 this manuscript, have no conflict of interest to declare.

221

222

## 223 **Legend of Figures**

224 **Figure 1:** Pain frequency maps generated by superimposing the pain drawings of all women with  
225 fibromyalgia syndrome (n=30). The colour bar represents the frequency of coloured areas. Dark red  
226 indicates the most frequently reported area of pain

227 **Figure 2:** Scatter plots of correlations between the total (A) and dorsal (B) are of pain extent with  
228 the worst pain experienced the preceding week (NPRS, 0-10) in women with fibromyalgia  
229 syndrome (n=30). Note that several points are overlapping. A positive linear regression line is fitted  
230 to the data.

231

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**Table 1:** Spearman's correlation coefficients between the pain extent, computed from pain drawings and quantitative sensory testing outcomes and clinical symptoms for women with fibromyalgia syndrome (n=30).

		Median (IQR)	Correlation with Pain extent ( $r_s$ )		
			Ventral	Dorsal	Total
	Age (years)	52 (12)	-.544**	.035	-.409*
	Pain duration (years)	8 (4.5)	-.367*	.336	-.017
	FIQ (0-100)	58.3 (13.5)	.262	-.147	.060
	Tender point count (0-18)	16 (4.25)	.031	.007	.016
NPRS (0-10)	Mean pain intensity	6 (2.0)	.110	.198	.272
	Worst level of pain	9 (1.0)	.212	.461*	.593**
	Lowest level of pain	4 (1.5)	-.008	.324	.215
PPT (kPa)	Suboccipital area	192 (53.5)	.056	-.196	-.118
	Mastoid process	205 (42.5)	-.005	-.197	-.218
	Trapezius muscle	185 (39)	-.159	.103	-.019
	Levator scapulae muscle	244 (50.2)	.127	-.151	-.065
	Posterior iliac crest	280 (64.5)	-.091	-.116	-.214
	Greater trochanter	275.5 (78.5)	-.040	.009	-.098
	Sternocostoclavicular joint	181.5 (46.7)	.055	-.036	-.38
	Wrist extensor muscles	225.5 (49.7)	.217	-.066	.053
	Knee (internal part)	205.5 (22.7)	-.168	-.040	-.233
	Second metacarpal	254.5 (55)	.082	.013	.044
	Tibialis anterior muscle	290.5 (57.7)	-.084	-.169	-.190
HPT (°C)	Cervical Spine	38.7 (2)	.190	-.192	.006
	Dorsal aspect of wrist	39.2 (2.3)	.206	.021	.124
	Tibialis anterior	40.4 (2.1)	.244	.047	.258
CPT (°C)	Cervical Spine	24.5 (5.1)	-.199	.153	-.006
	Dorsal aspect of wrist	23.9 (4.6)	-.360	.095	-.215
	Tibialis anterior	24.5 (4.5)	-.406*	.226	-.147

NPRS: Numerical Pain Rating Scale; FIQ: Fibromyalgia Impact Questionnaire;  
PPT: Pressure Pain Threshold; CPT: Cold Pain Threshold; HPT: Heat Pain Threshold  
IQR: Inter Quartile Range;  $r_s$ : Spearman's rho

\* Significant at the 0.05 level (2-tailed)

\*\* Significant at the 0.001 level (2-tailed)